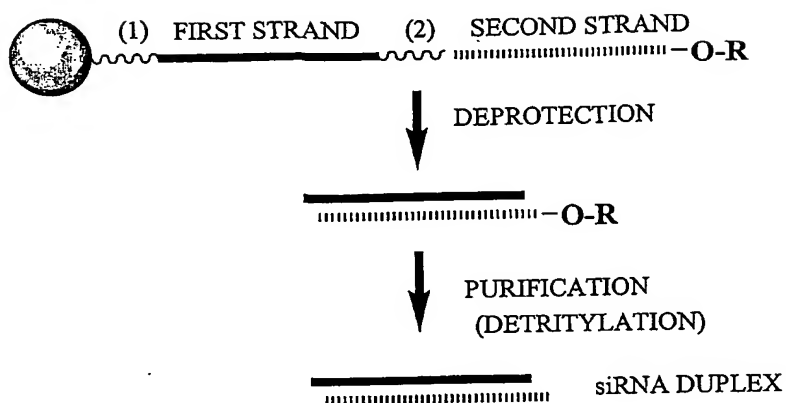


1/29

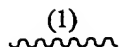
**Figure 1**

= SOLID SUPPORT

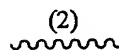
R = TERMINAL PROTECTING GROUP

FOR EXAMPLE:

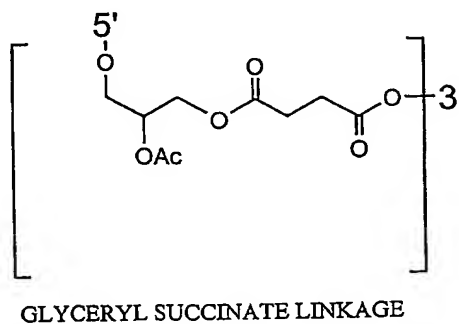
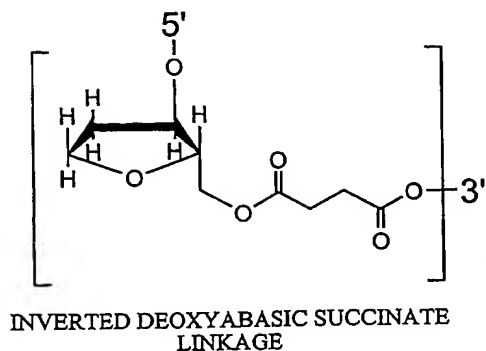
DIMETHOXYTRITYL (DMT)



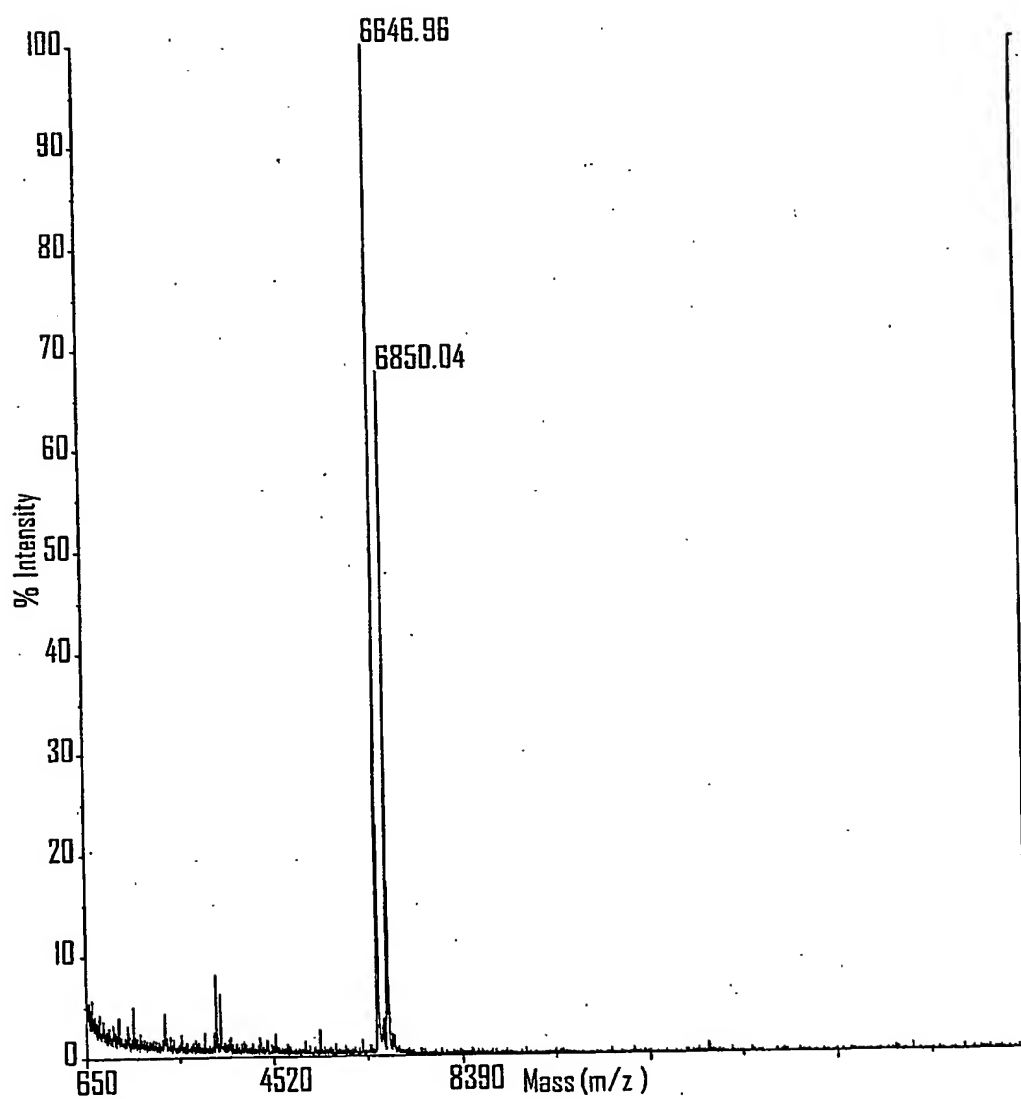
= CLEAVABLE LINKER

(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR  
INVERTED DEOXYABASIC SUCCINATE)

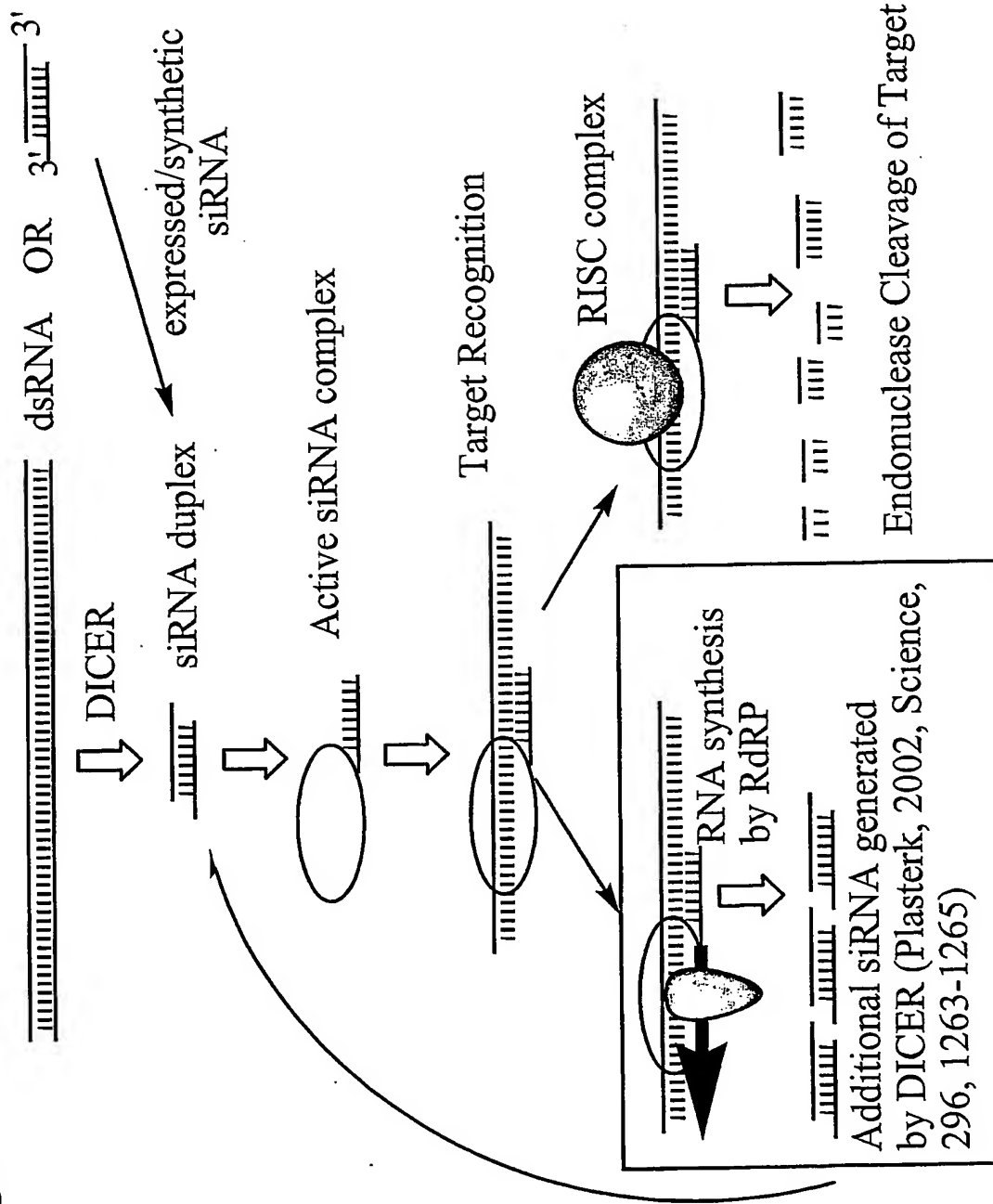
= CLEAVABLE LINKER

(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR  
INVERTED DEOXYABASIC SUCCINATE)

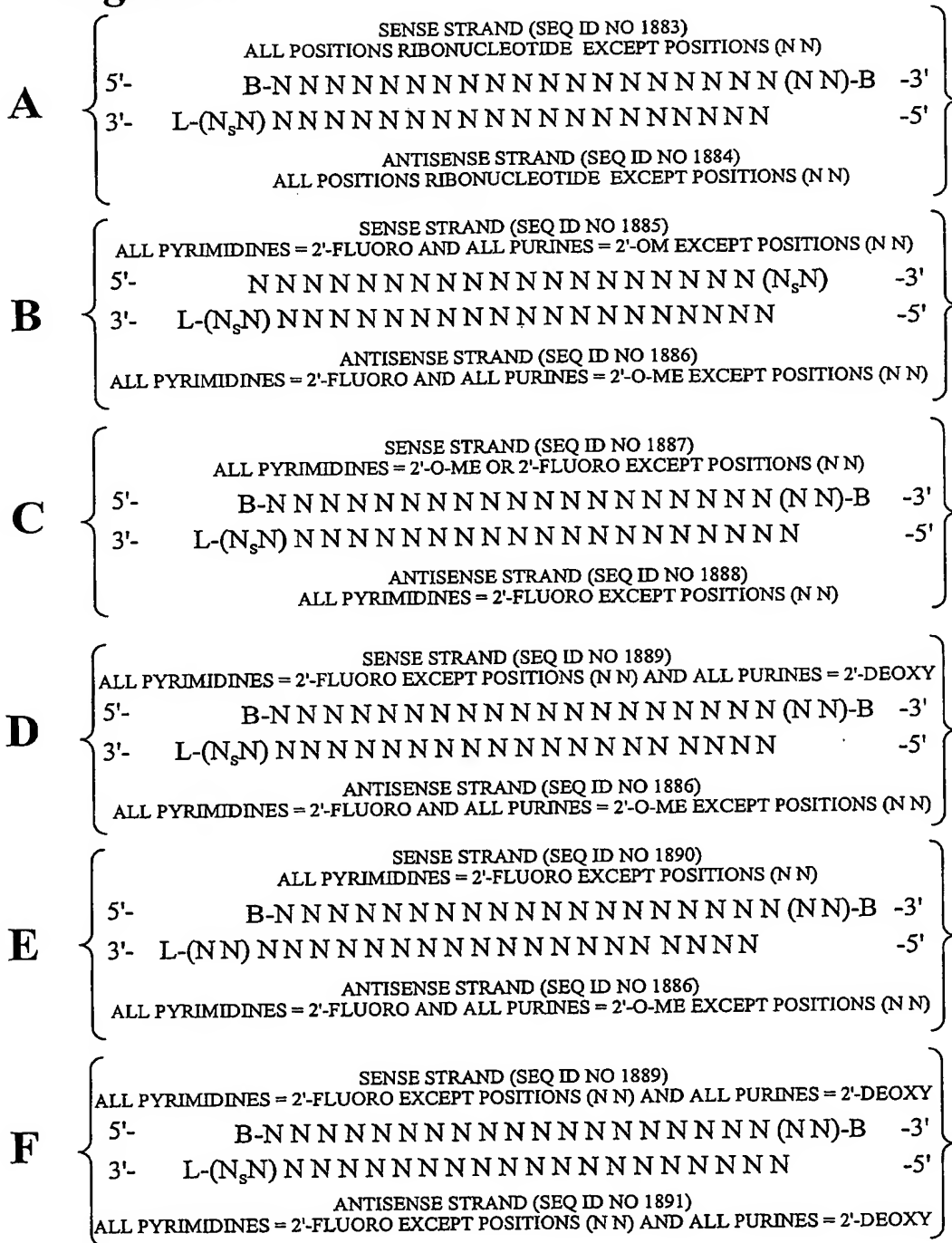
2/29

*Figure 2*

**Figure 3**

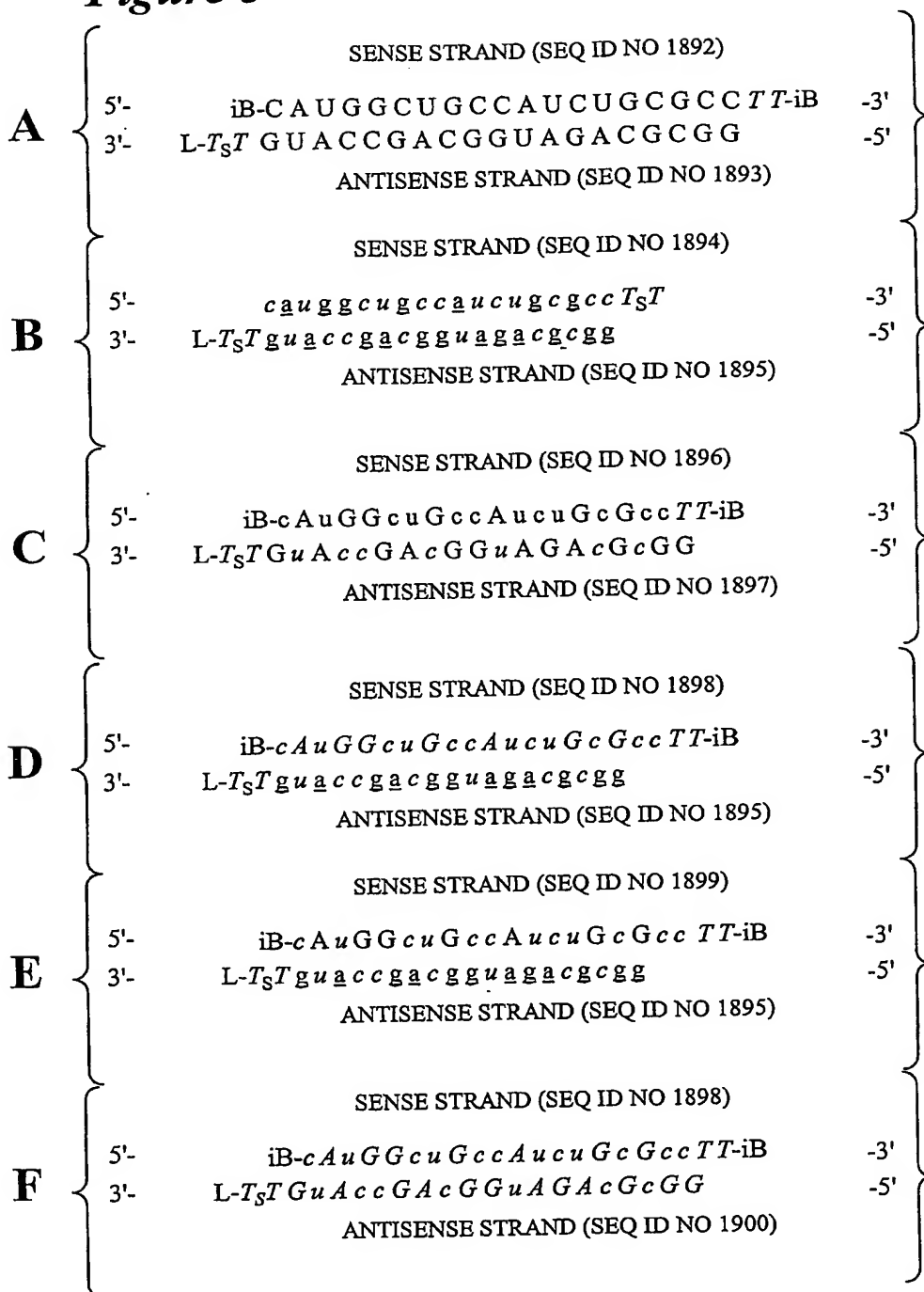


4/29

**Figure 4**

POSITIONS (NN) CAN COMPRISE ANY NUCLEOTIDE, SUCH AS DEOXYNUCLEOTIDES (eg. THYMIDINE) OR UNIVERSAL BASES  
 B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP THAT IS OPTIONALLY PRESENT  
 L = GLYCERYL OR B THAT IS OPTIONALLY PRESENT  
 S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE THAT IS OPTIONALLY ABSENT

5/29

**Figure 5**

lower case = 2'-O-Methyl or 2'-deoxy-2'-fluoro

*italic lower case* = 2'-deoxy-2'-fluorounderline = 2'-O-methyl*ITALIC UPPER CASE* = DEOXY

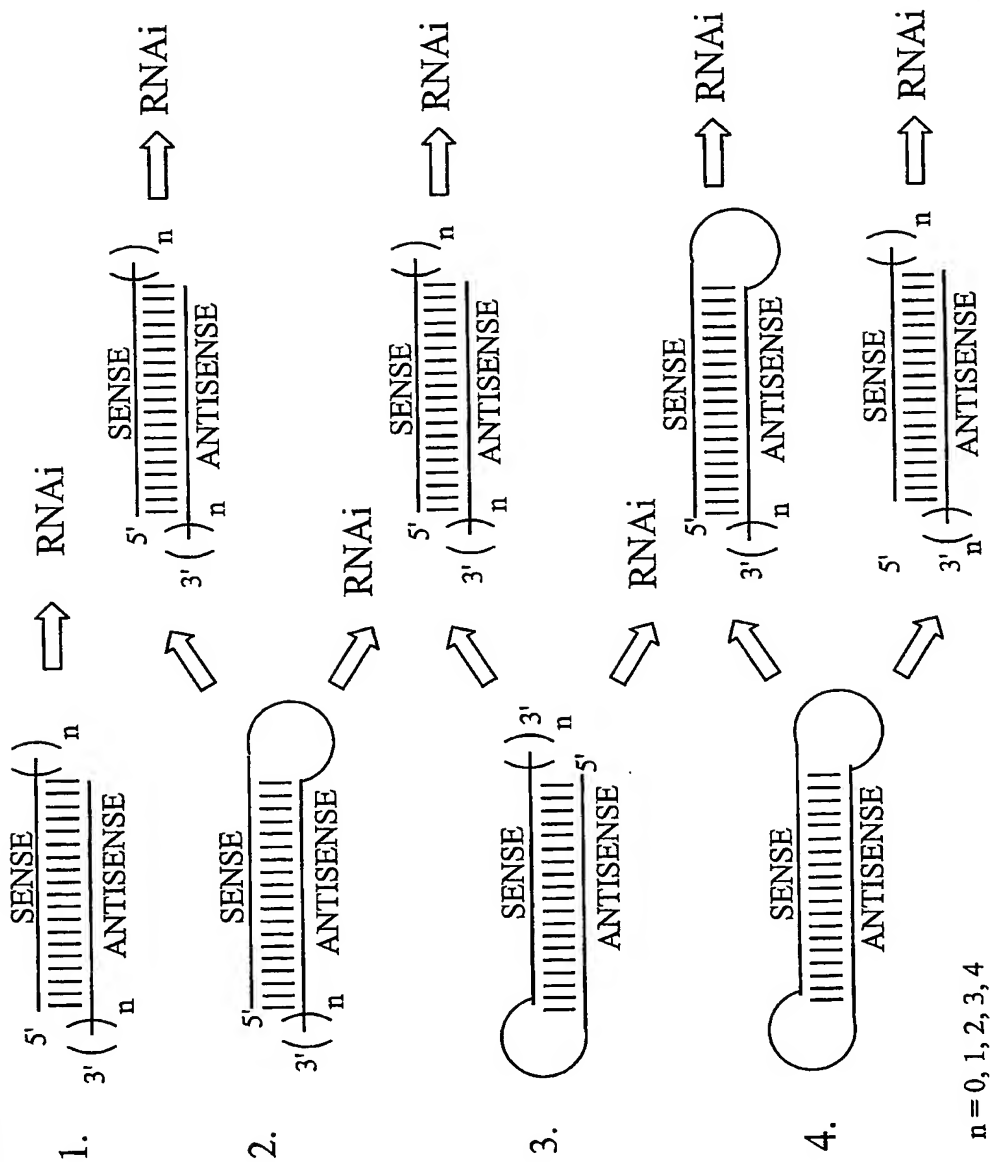
iB = INVERTED DEOXYABASIC

L = GLYCERYL MOIETY OR iB OPTIONALLY PRESENT

S = PHOSPHOROTHIOATE OR

PHOSPHORODITHIOATE OPTIONALLY PRESENT

**Figure 6**



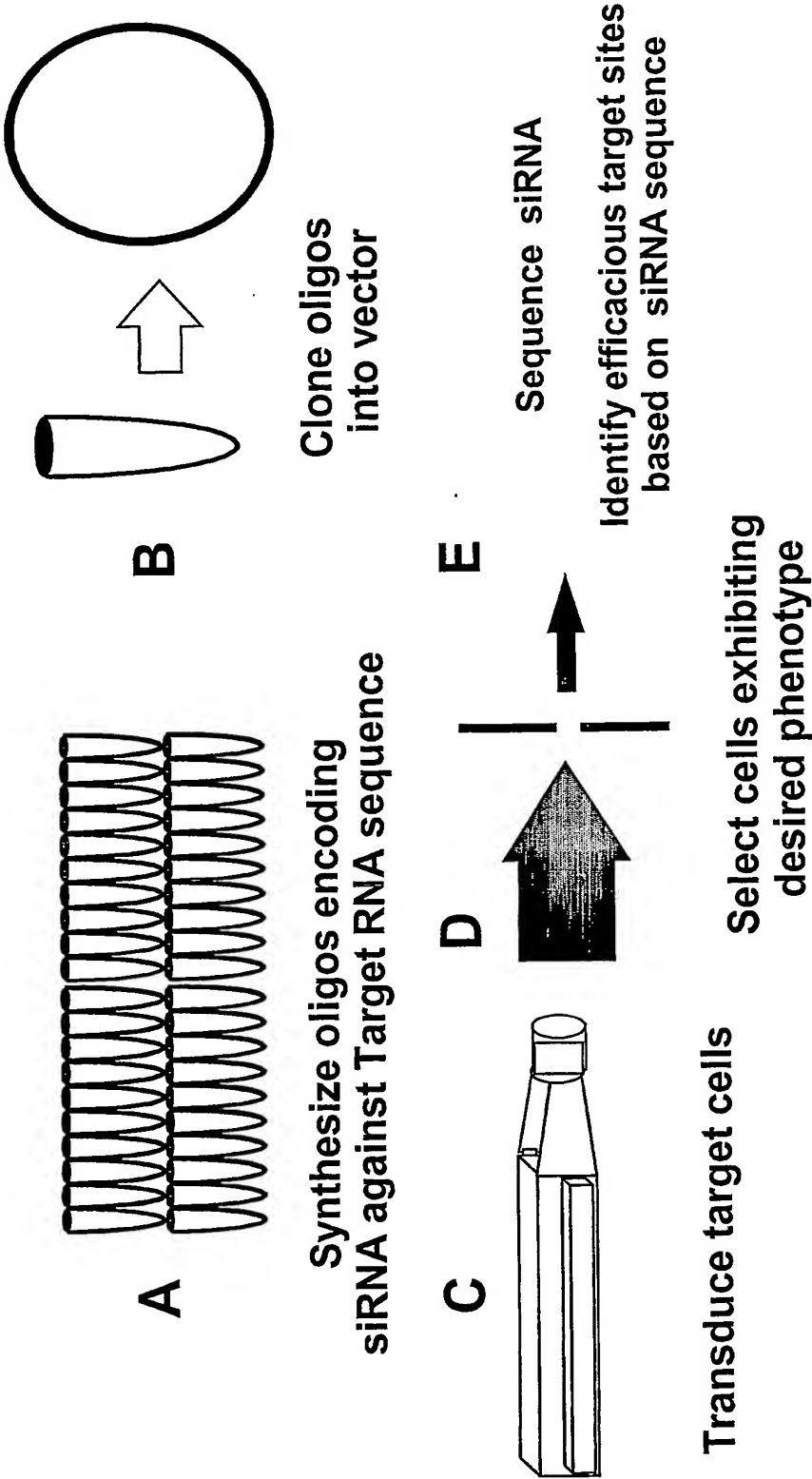




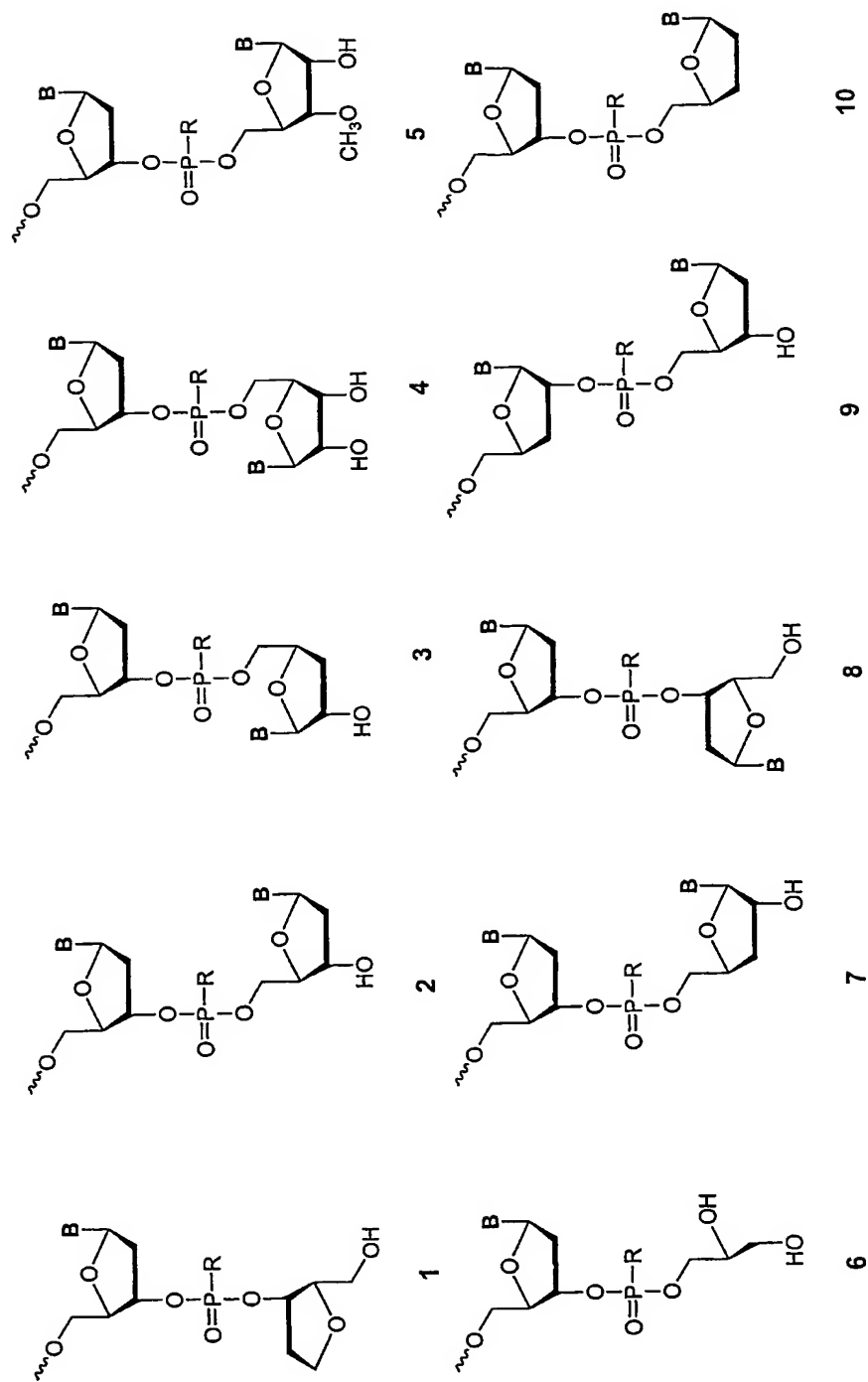


9/29

Figure 9: Target site Selection using siRNA



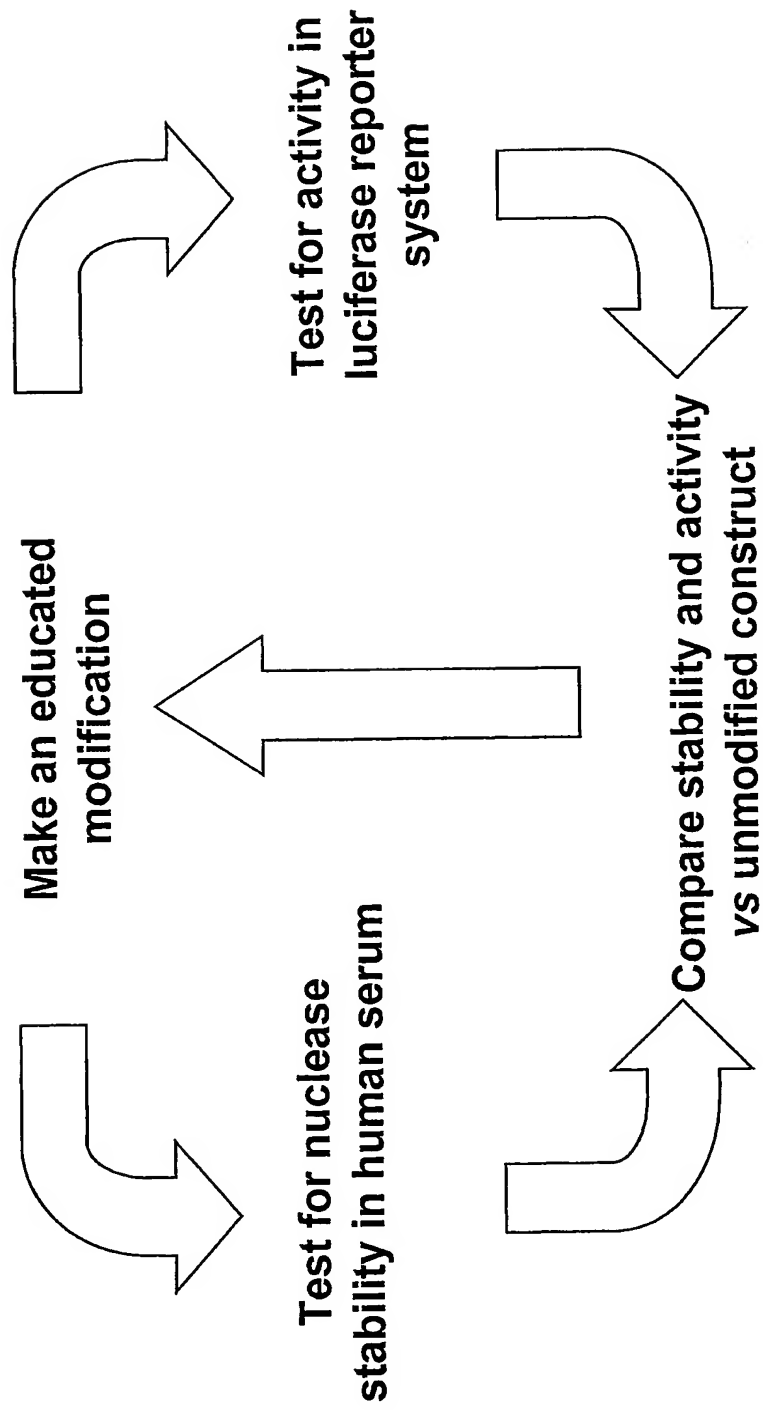
10/29

**Figure 10**

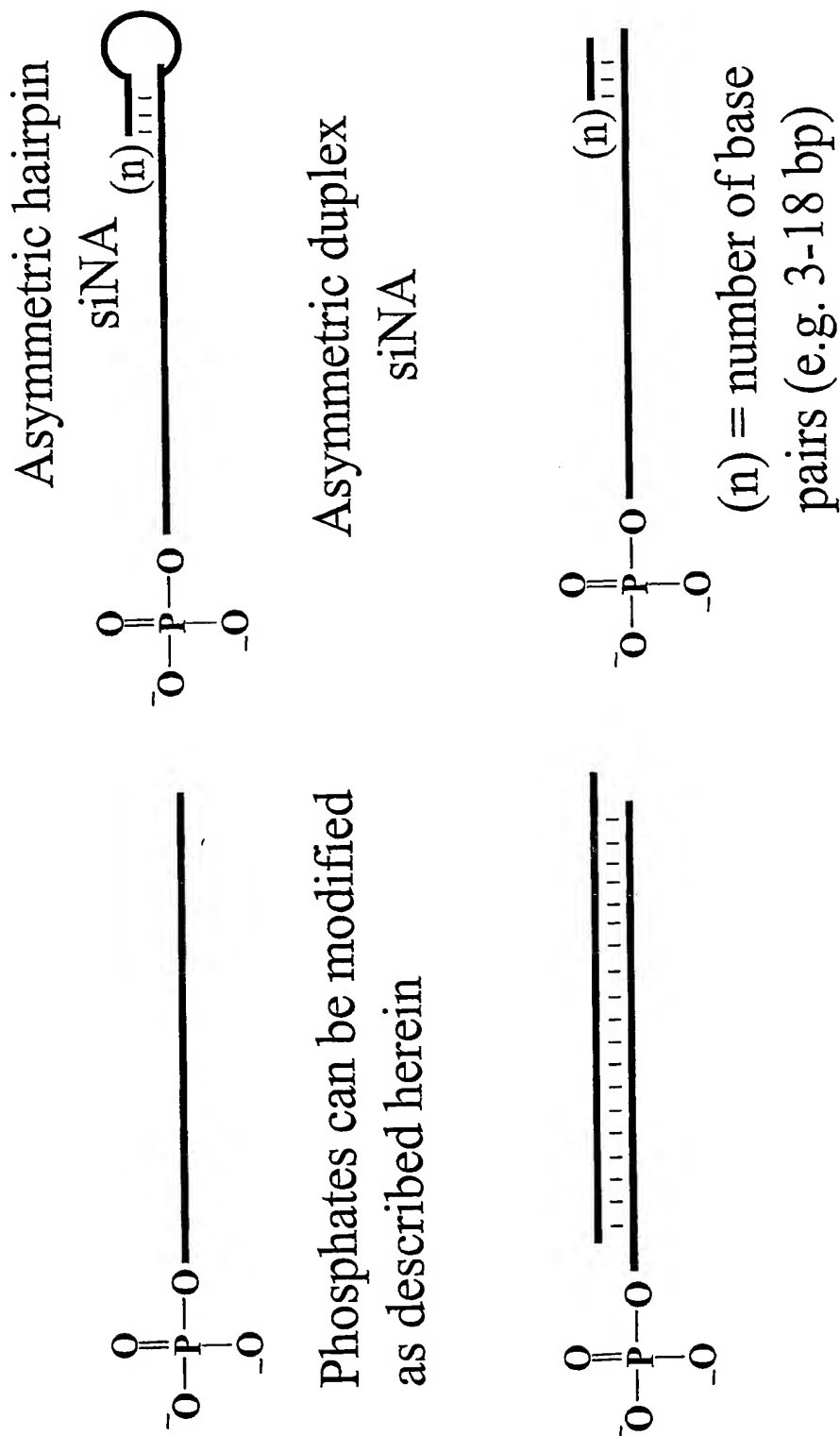
R = O, S, N, alkyl, substituted alkyl, O-alkyl, S-alkyl, alkaryl, or aralkyl  
B = Independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).

11/29

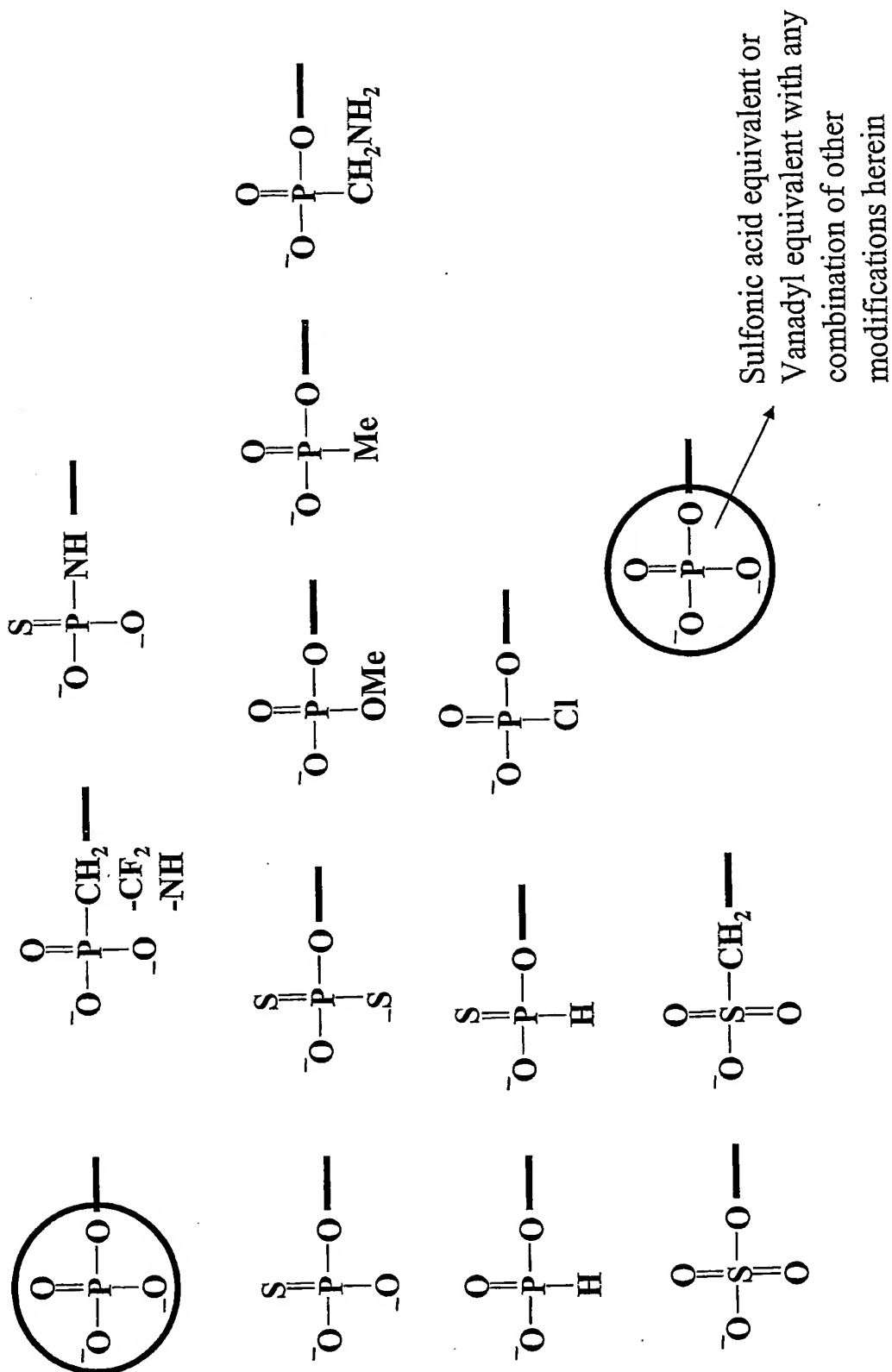
**Figure 11: Modification Strategy**

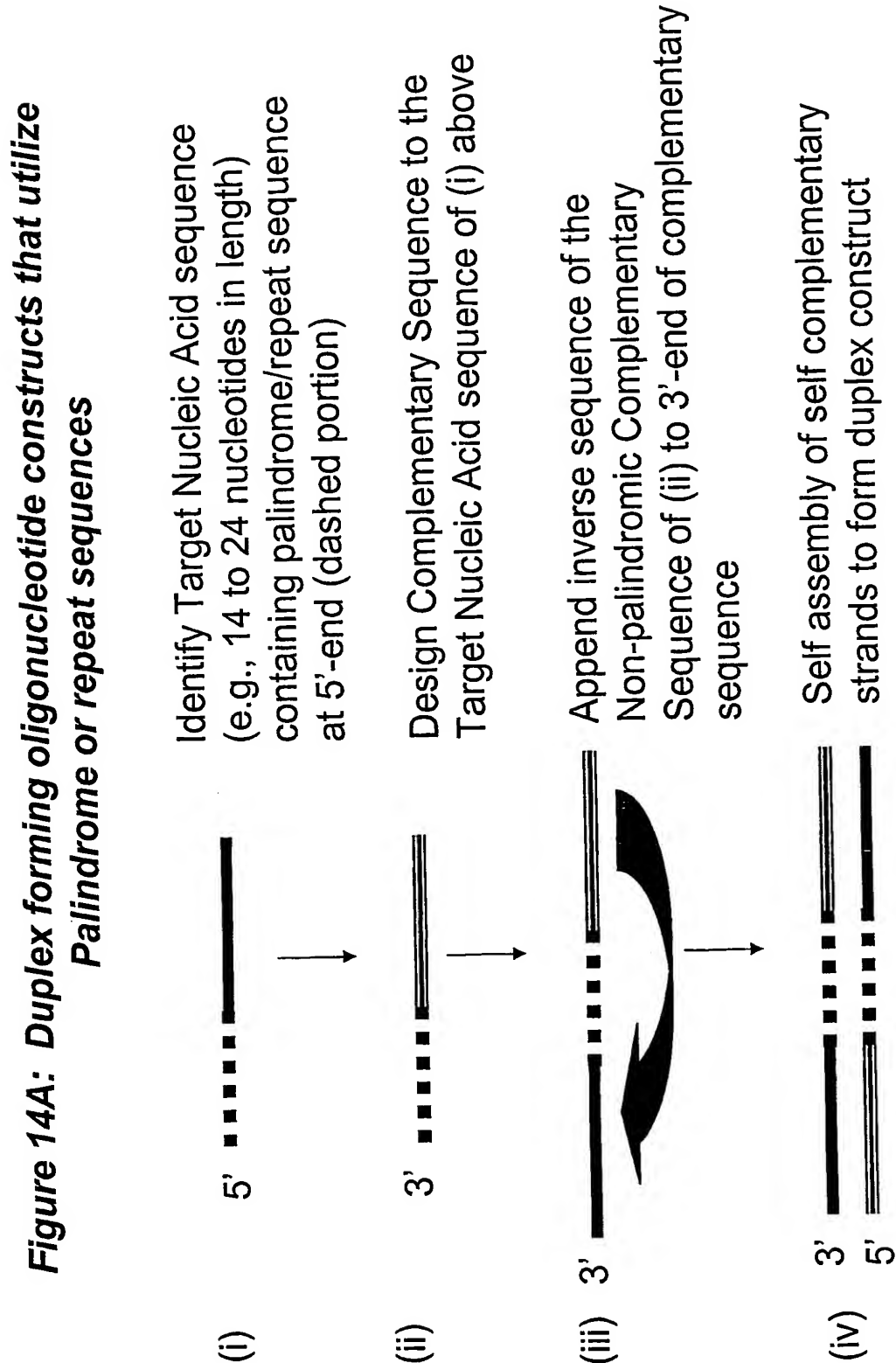


12/29

*Figure 12: Phosphorylated siNA constructs*

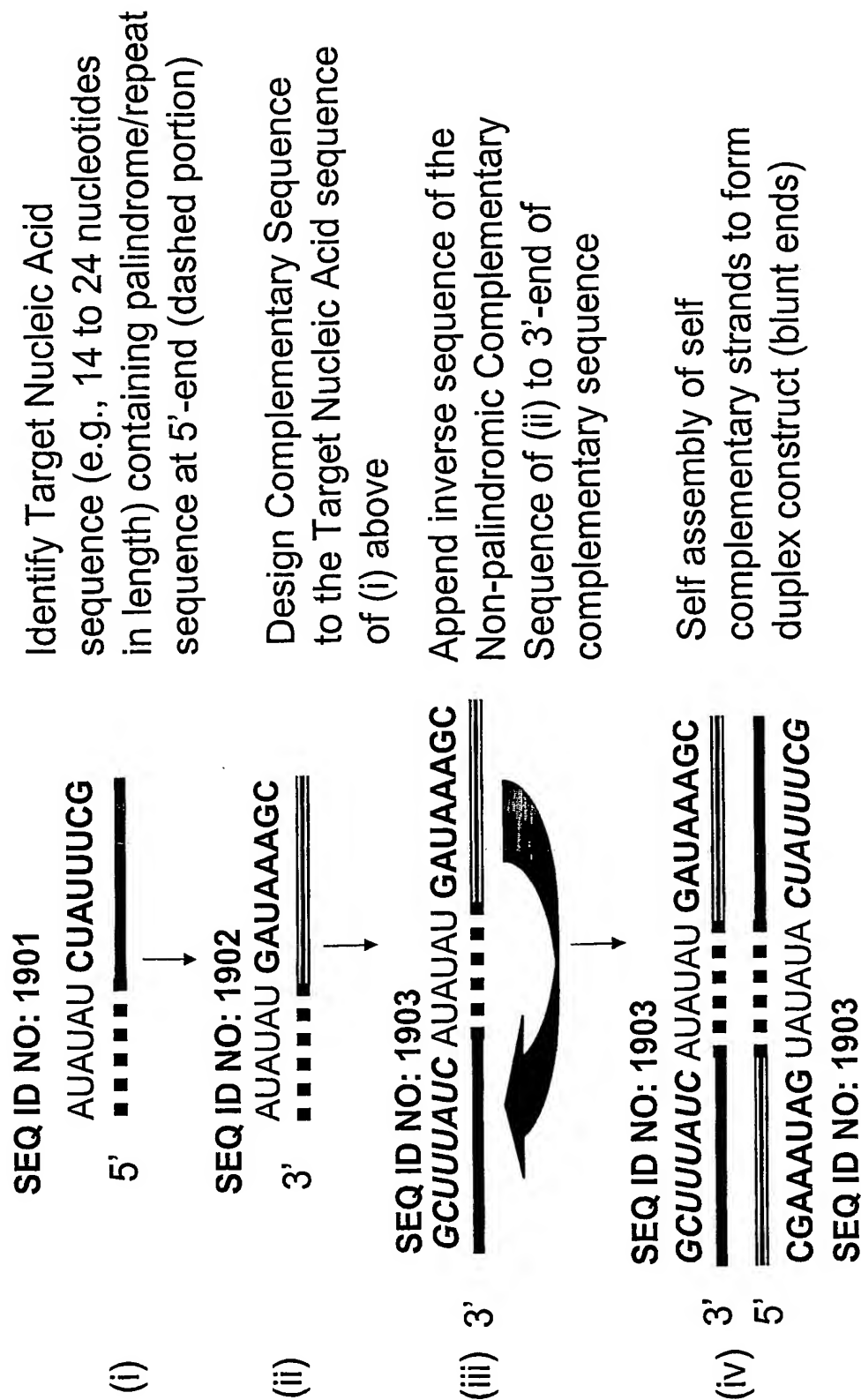
13/29

*Figure 13: 5'-phosphate modifications*

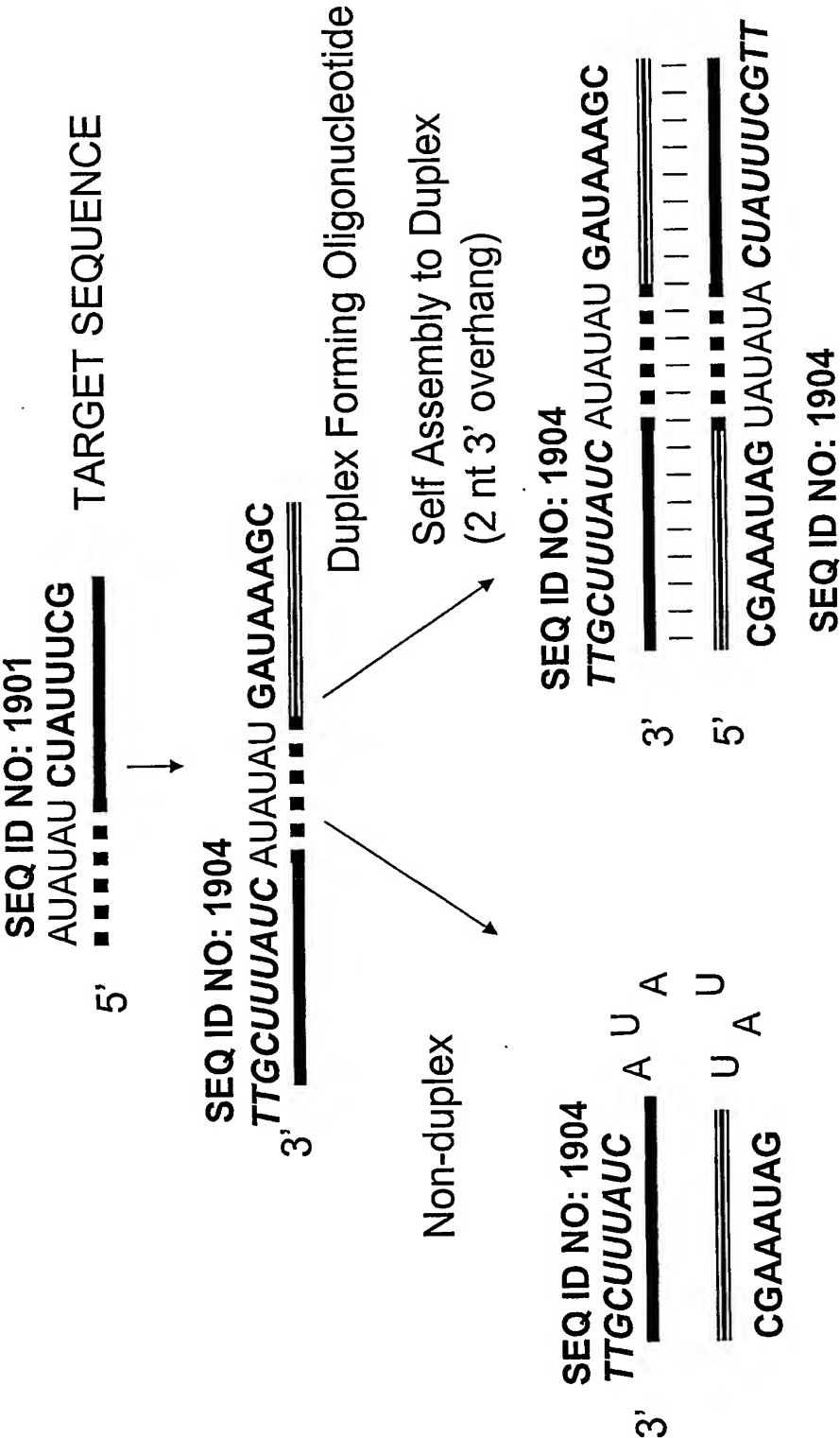


15/29

**Figure 14B: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence**

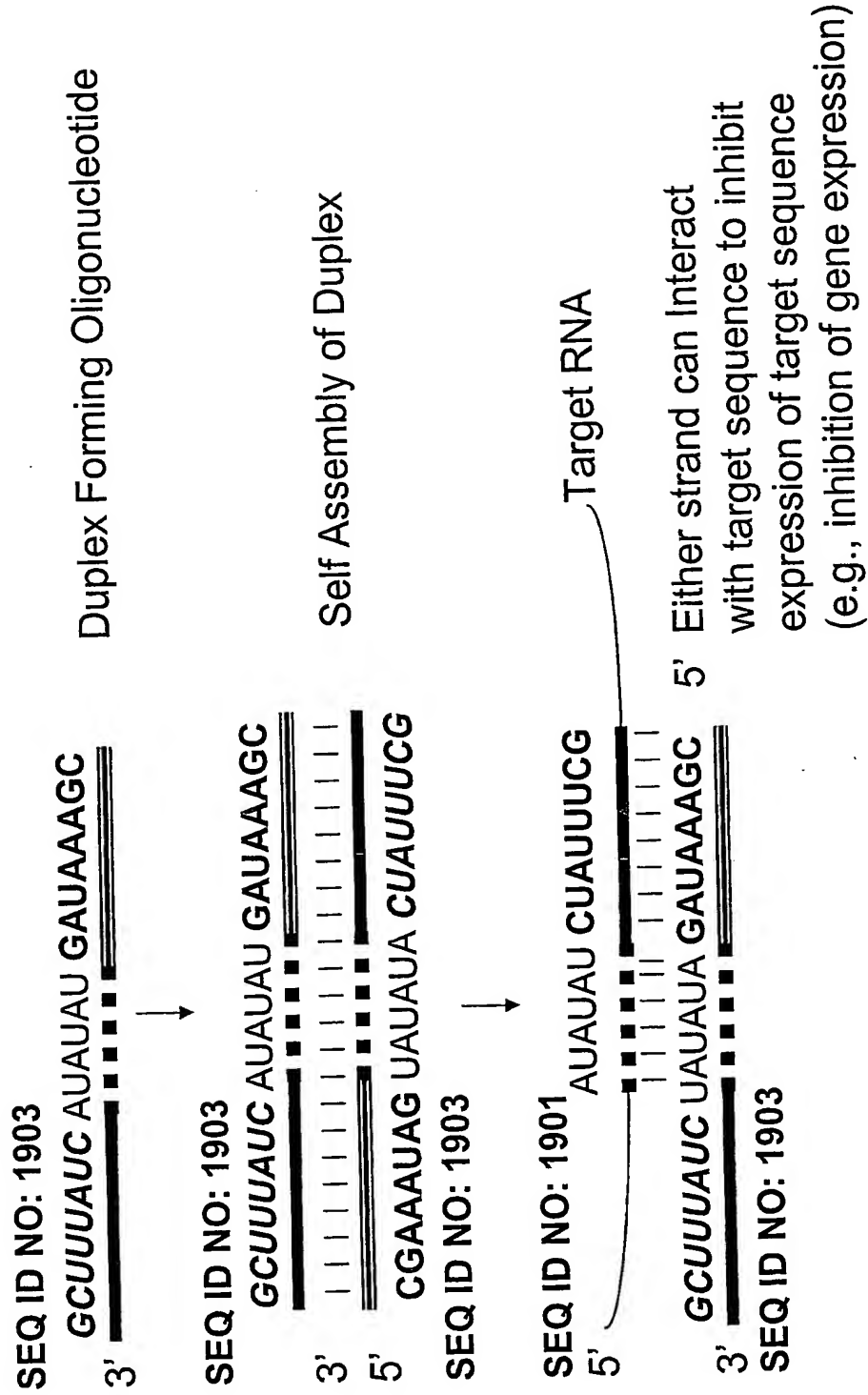


**Figure 14C: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly**

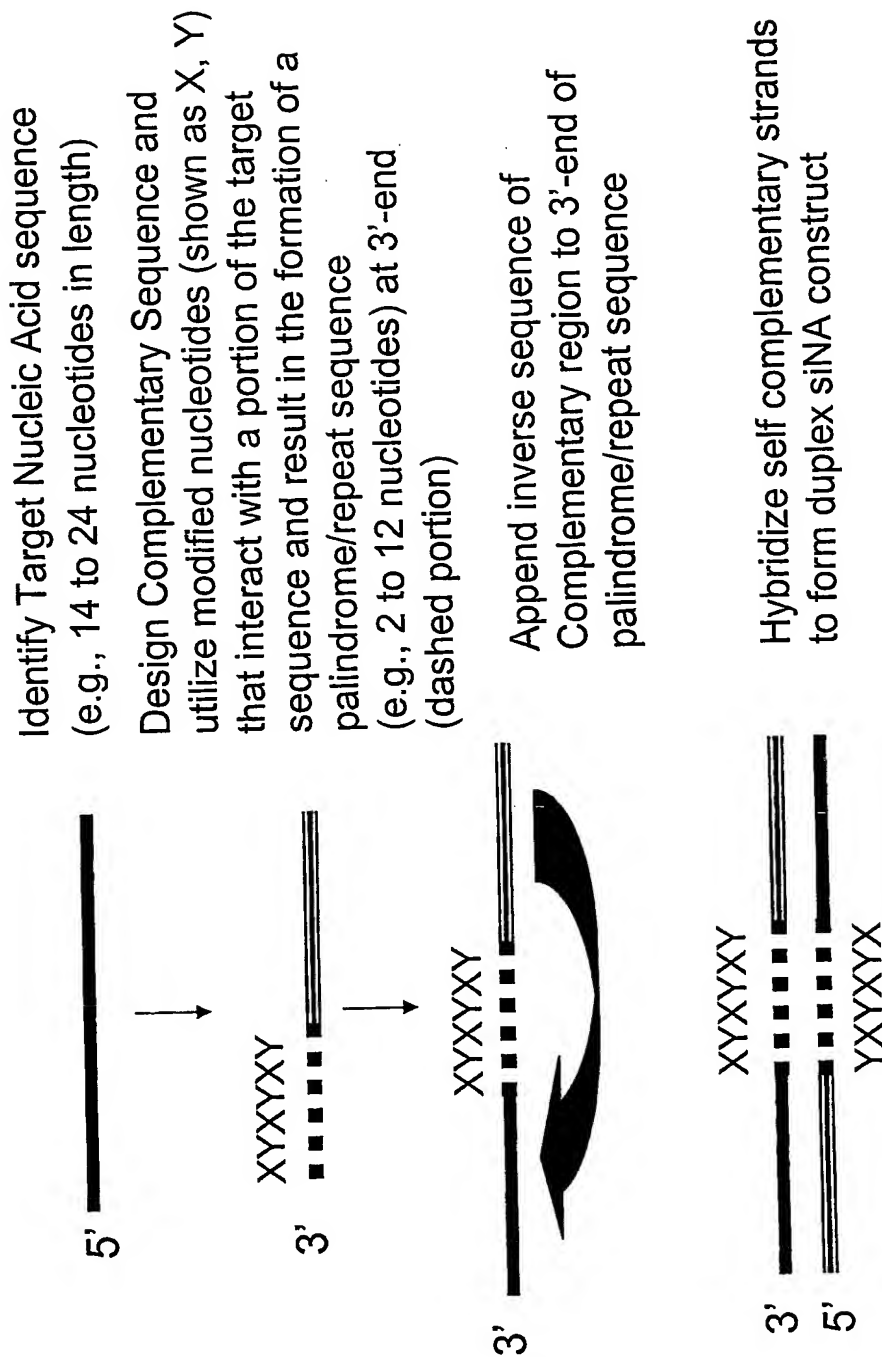




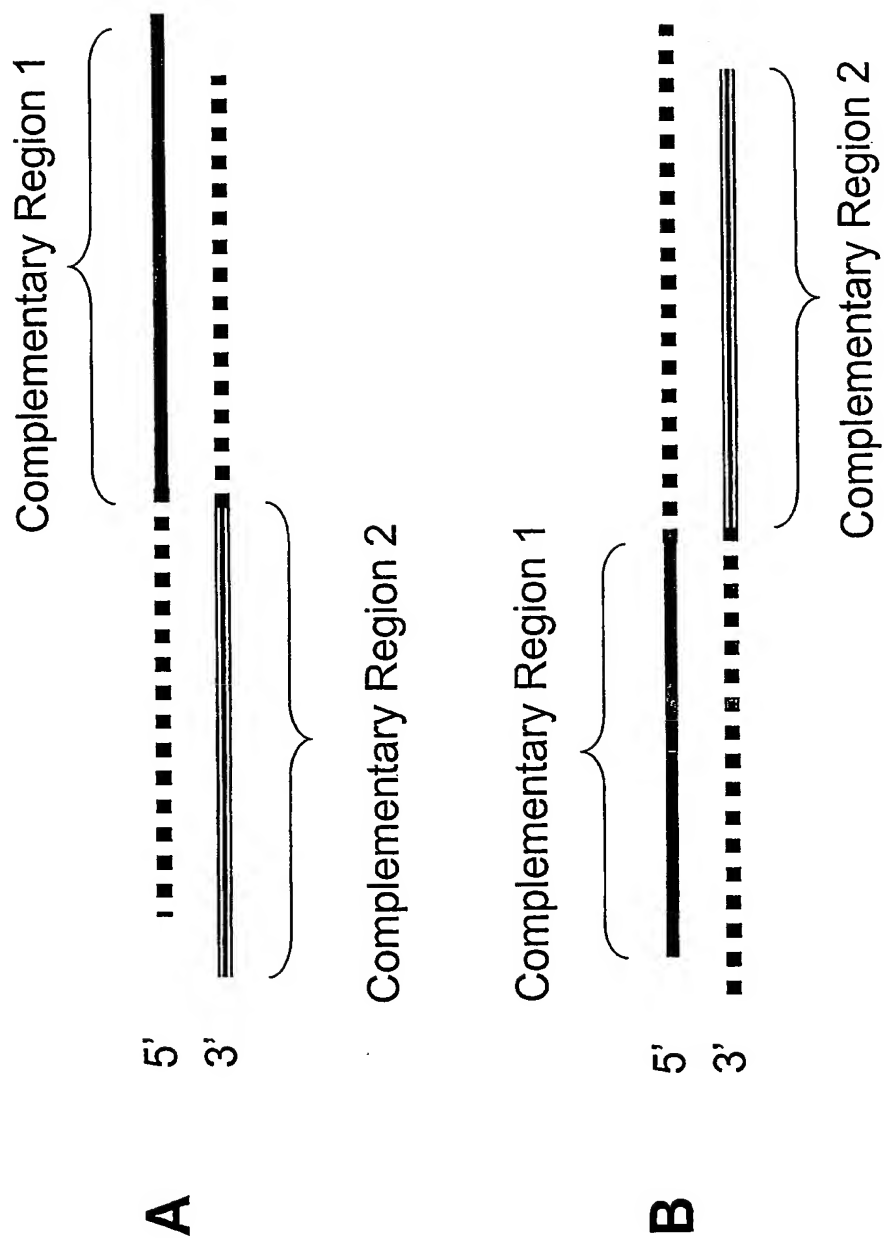
**Figure 14D: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly and inhibition of Target Sequence Expression**



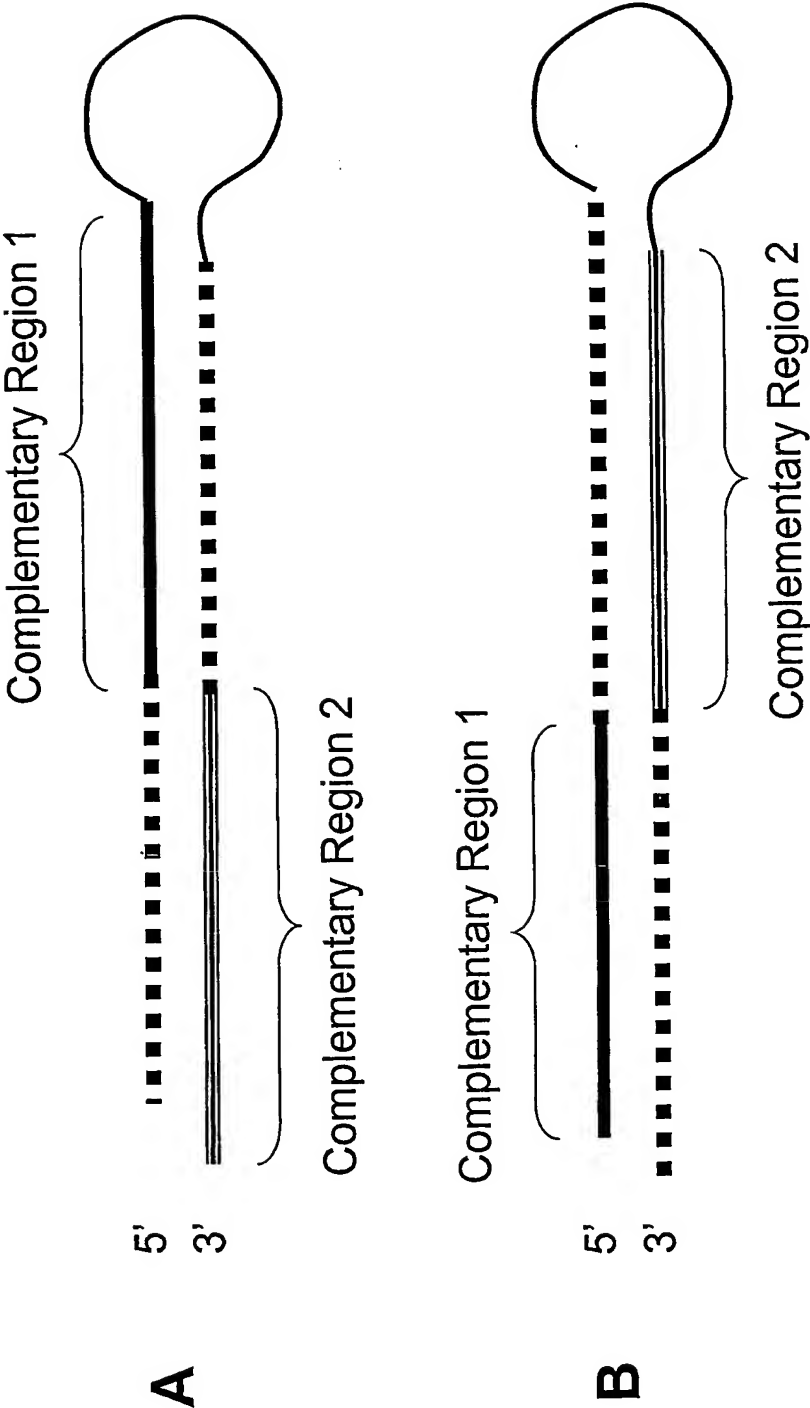
**Figure 15: Duplex forming oligonucleotide constructs that utilize artificial palindrome or repeat sequences**



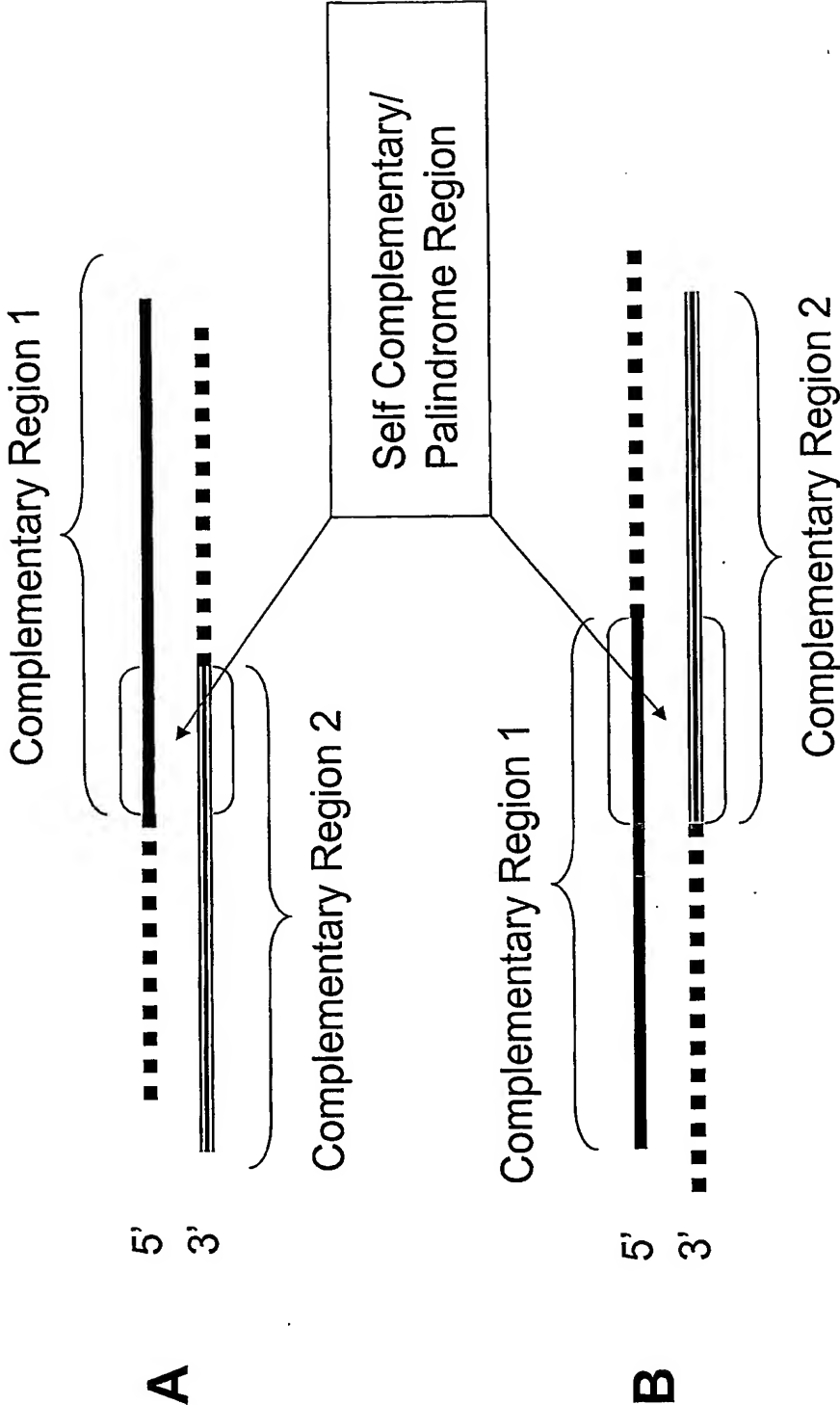
**Figure 16: Examples of double stranded multifunctional siNA constructs with distinct complementary regions**



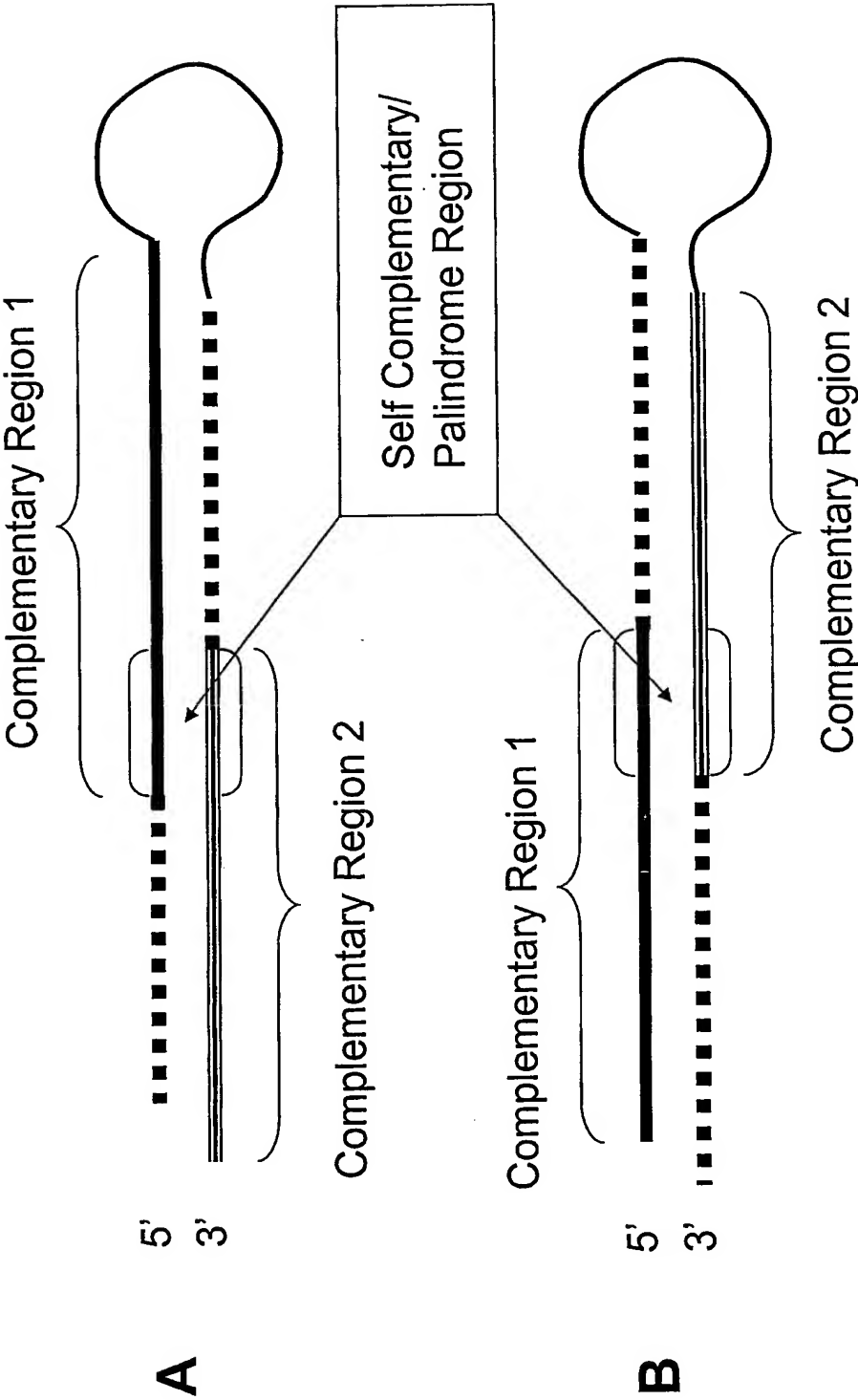
**Figure 17: Examples of hairpin multifunctional siNA constructs with distinct complementary regions**



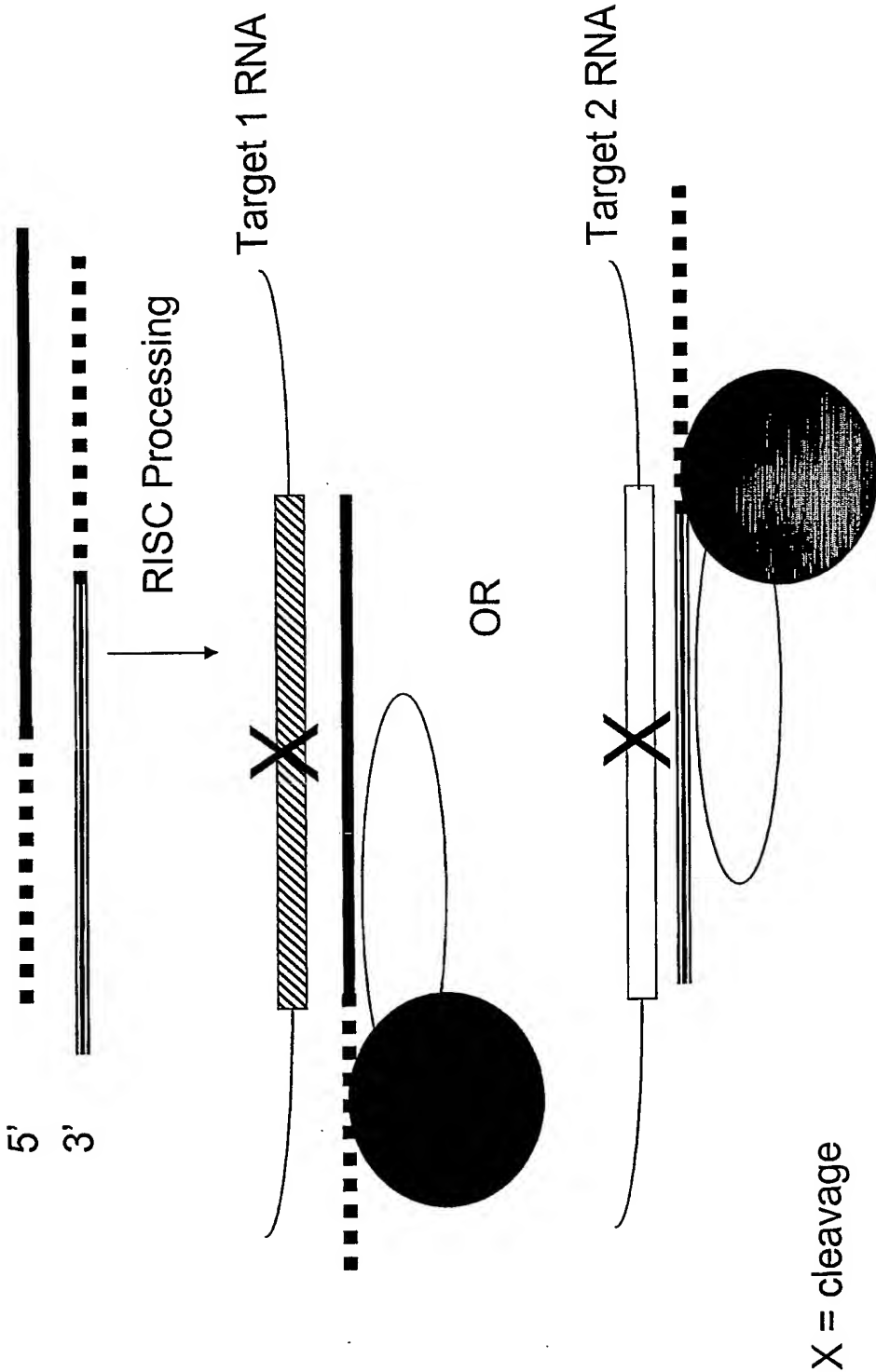
**Figure 18:** Examples of double stranded multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region



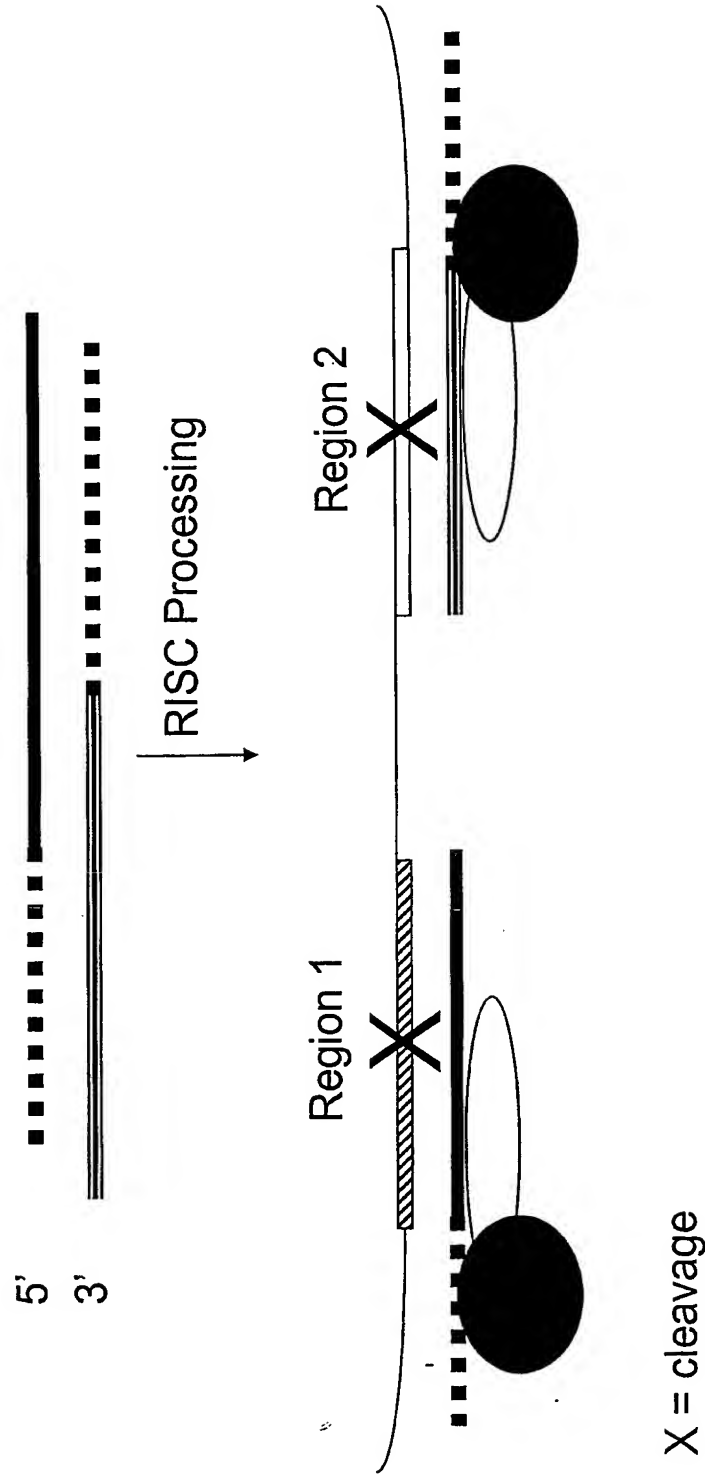
**Figure 19: Examples of hairpin multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region**



**Figure 20: Example of multifunctional siNA targeting two  
Separate Target nucleic acid sequences**



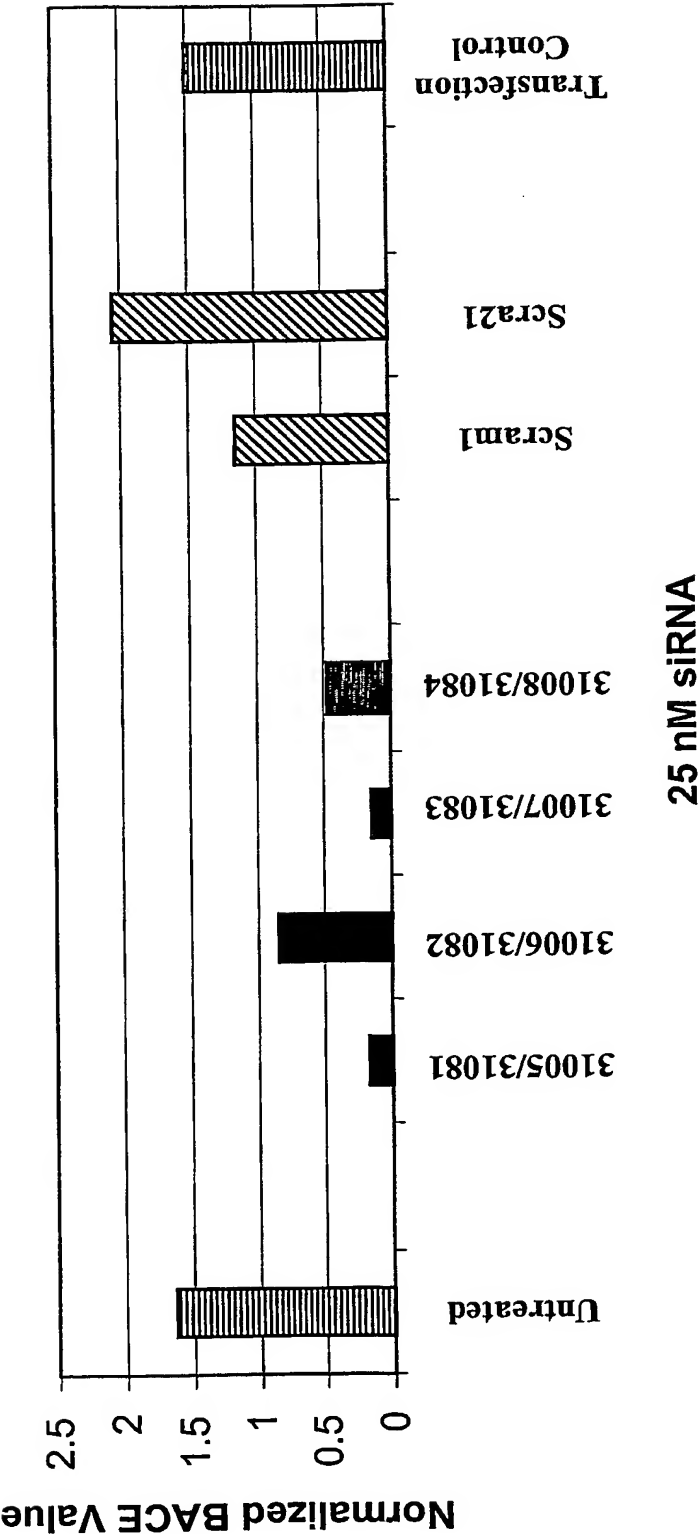
**Figure 21:** *Example of multifunctional siNA targeting two regions within the same target nucleic acid sequence*





25/29

Figure 22: A549 24h BACE mRNA Expression



26/29

**Figure 23: A549 24h BACE mRNA Expression  
using modified siNA**

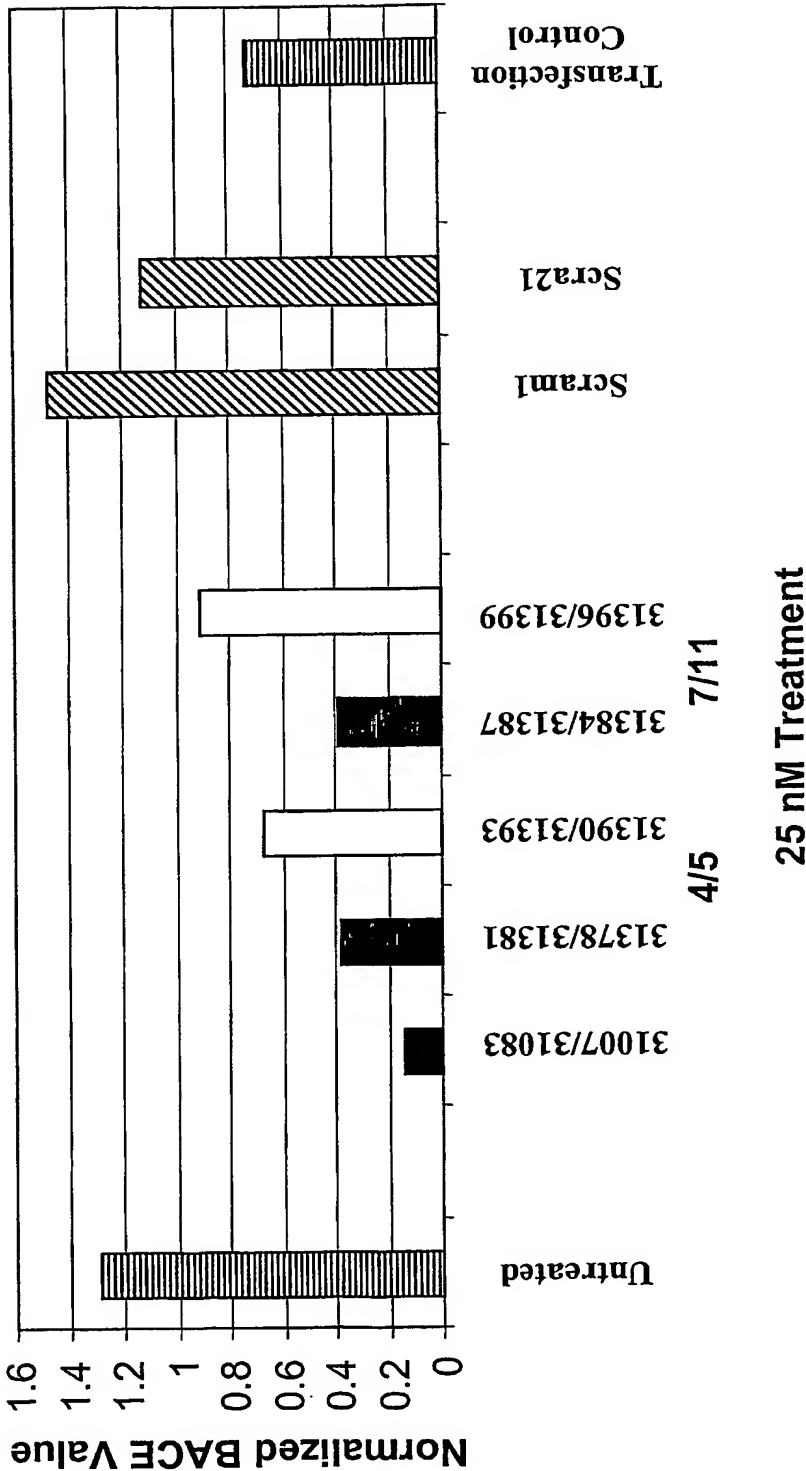
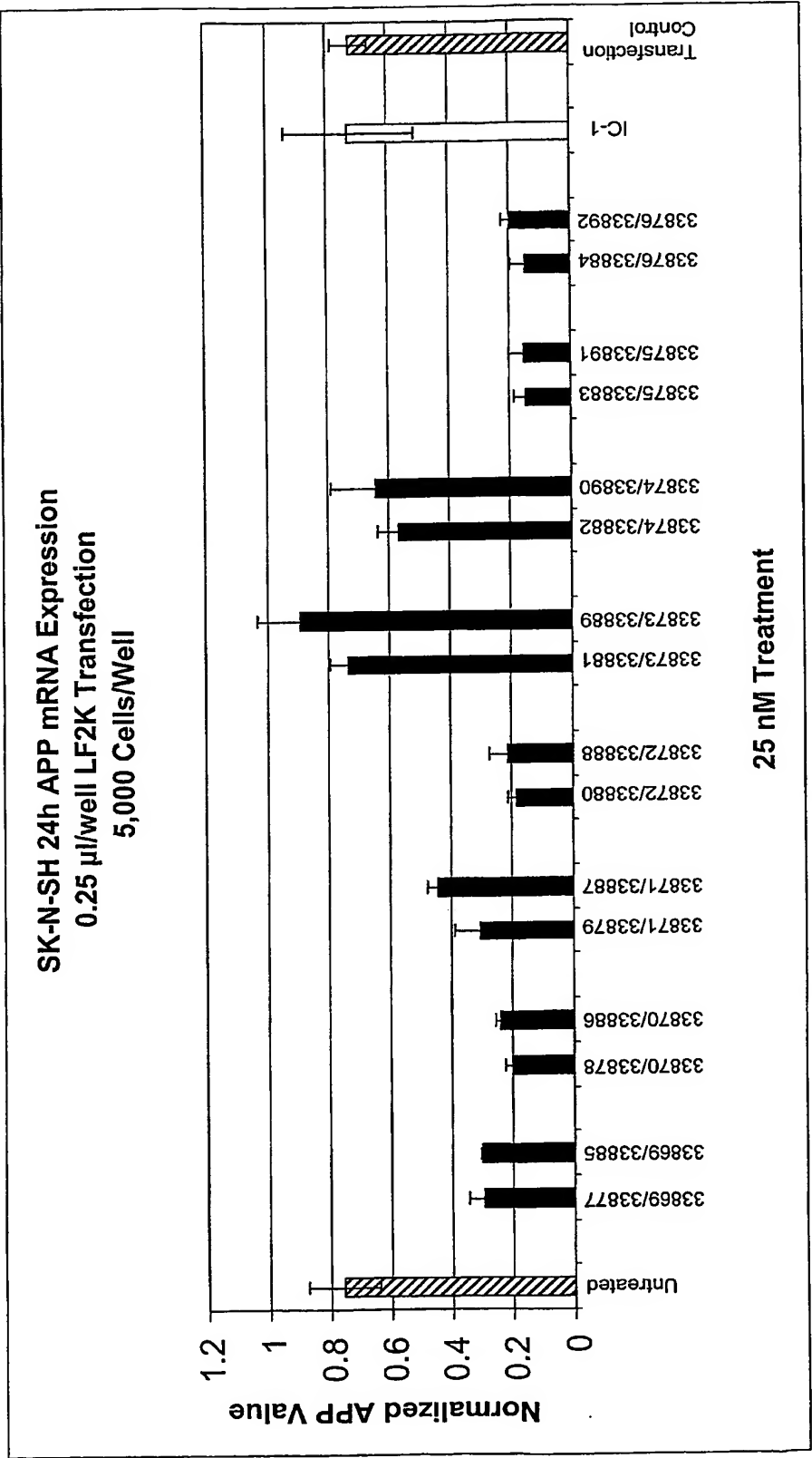


FIGURE 24



28/29

**FIGURE 25**

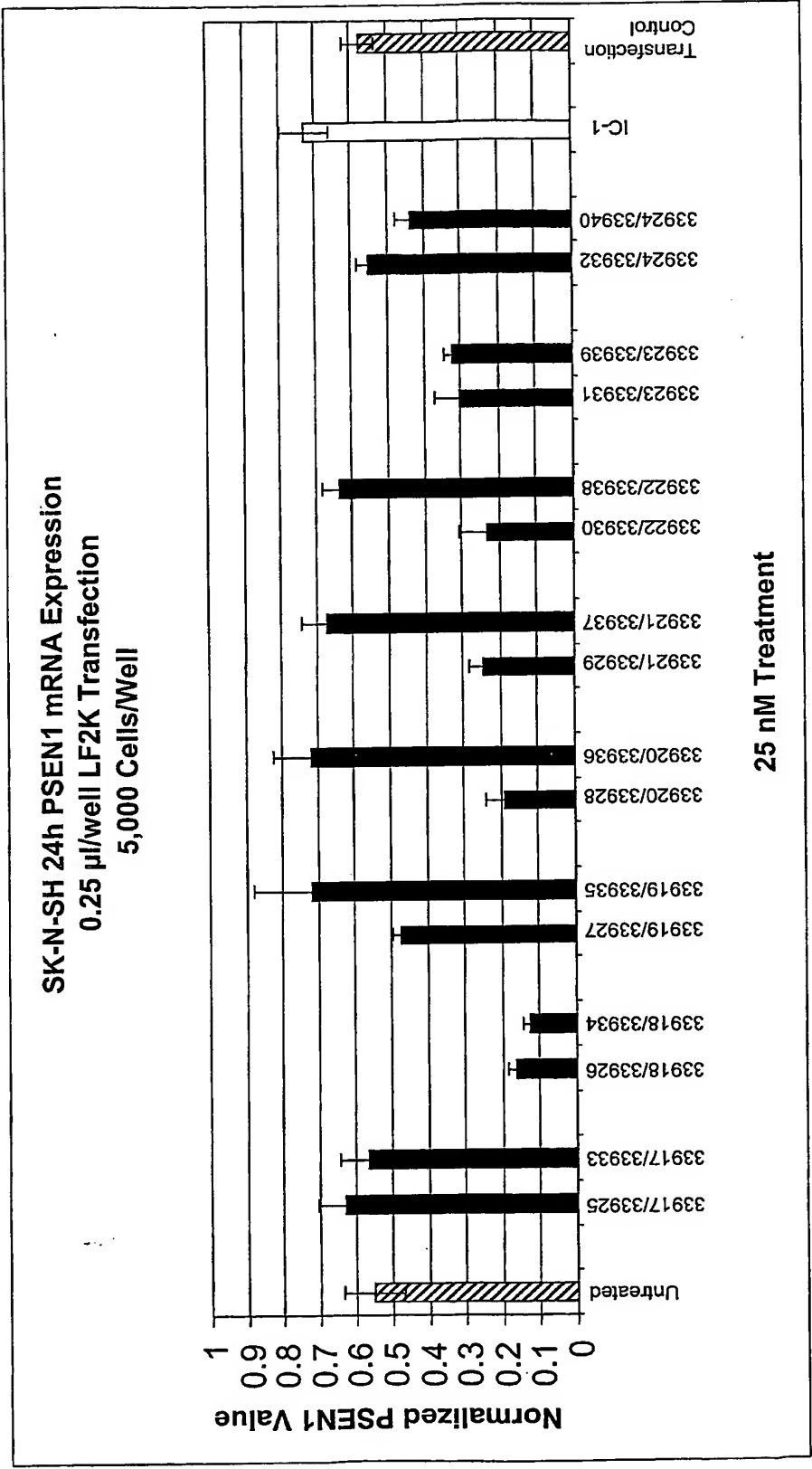


FIGURE 26

